Fate of iPSCs Derived from Azoospermic and Fertile Men following Xenotransplantation to Murine Seminiferous Tubules.

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Public Summary:
This work demonstrates the potential feasibility of using iPSCs for treatment of male infertility linked to genetic causes, treatments linked to cancer or unexplained infertility.

Scientific Abstract:
Historically, spontaneous deletions and insertions have provided means to probe germline developmental genetics in Drosophila, mouse and other species. Here, induced pluripotent stem cell (iPSC) lines were derived from infertile men with deletions that encompass three Y chromosome azoospermia factor (AZF) regions and are associated with production of few or no sperm but normal somatic development. AZF-deleted iPSC lines were compromised in germ cell development in vitro. Undifferentiated iPSCs transplanted directly into murine seminiferous tubules differentiated extensively to germ-cell-like cells (GCLCs) that localized near the basement membrane, demonstrated morphology indistinguishable from fetal germ cells, and expressed germ-cell-specific proteins diagnostic of primordial germ cells. Alternatively, all iPSCs that exited tubules formed primitive tumors. iPSCs with AZF deletions produced significantly fewer GCLCs in vivo with distinct defects in gene expression. Findings indicate that xenotransplantation of human iPSCs directs germ cell differentiation in a manner dependent on donor genetic status.